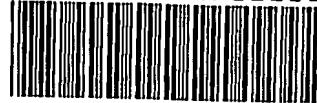


Translation

PATENT COOPERATION TREATY

PCT

PCT Application
PCT/CN2004/000591



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference FPCH04160022		FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/CN2004/000591	International filing date (day/month/year) 02 Jun, 2004 (02.06.2004)	Priority date (day/month/year) 02 Jun, 2003 (02.06.2003)	
International Patent Classification (IPC) or national classification and IPC IPC7: C07D471/04, A61P35/00			
Applicant XINJIANG HUASHIDAN PHARMACEUTICAL RESEARCH CO. LTD, ET AL.			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (sent to the applicant and to the International Bureau) a total of 24 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic _____), containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 29. Dec. 2004 (29.12.2004)		Date of completion of this report 13. Sep. 2005 (13.09.2005)	
Name and mailing address of the IPEA/CN The State Intellectual Property Office, the P.R.China, 6 Xitucheng Rd., Jimen Bridge, Haidian District, Beijing, China 100088 Facsimile No. 86-10-62019451		Authorized officer 来汪印送 Telephone No. (86-10): 62085593	

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/CN2004/000591

Box No. I Basis of the report

1. With regard to the language, this report is based on:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rules 12.3(a) and 23.1(b))
- ☐ publication of the international application (Rule 12.4(a))
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☐ the international application as originally filed/furnished
- ☒ the description:
- | | | |
|---------|---|--|
| pages | <u>1-19,21-23,27-58,61-63,66-75,78-96</u> | as originally filed/furnished |
| pages * | <u>20,24-26,59-60,64-65,76-77</u> | received by this Authority on <u>29. Dec. 2004</u> |
| pages * | _____ | received by this Authority on _____ |
- ☒ the claims:
- | | | |
|---------|----------------|---|
| pages | _____ | as originally filed/furnished |
| pages * | _____ | as amended (together with any statement) under Article 19 |
| pages * | <u>97-103G</u> | received by this Authority on <u>29. Dec. 2004</u> |
| pages * | _____ | received by this Authority on _____ |
- ☒ the drawings:
- | | | |
|---------|-------------|-------------------------------------|
| pages | <u>1-15</u> | as originally filed/furnished |
| pages * | _____ | received by this Authority on _____ |
| pages * | _____ | received by this Authority on _____ |
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

4. ☒ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☒ the claims, Nos. 1-58, 61-68, 70-72, 75-84
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/CN2004/000591

Box No. I Basis of the report

1. With regard to the language, this report is based on:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rules 12.3(a) and 23.1(b))
- ☐ publication of the international application (Rule 12.4(a))
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☐ the international application as originally filed/furnished
- ☒ the description:
- | | | |
|---------|---|--|
| pages | <u>1-19,21-23,27-58,61-63,66-75,78-96</u> | as originally filed/furnished |
| pages * | <u>20,24-26,59-60,64-65,76-77</u> | received by this Authority on <u>29. Dec. 2004</u> |
| pages * | _____ | received by this Authority on _____ |
- ☒ the claims:
- | | | |
|---------|-----------------|---|
| pages | <u>97-103</u> | as originally filed/furnished |
| pages * | _____ | as amended (together with any statement) under Article 19 |
| pages * | <u>6, 9, 13</u> | received by this Authority on <u>29. Dec. 2004</u> |
| pages * | _____ | received by this Authority on _____ |
- ☒ the drawings:
- | | | |
|---------|-------------|-------------------------------------|
| pages | <u>1-15</u> | as originally filed/furnished |
| pages * | _____ | received by this Authority on _____ |
| pages * | _____ | received by this Authority on _____ |
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☒ the claims, Nos. 25-26,28-30,32,35-58,61-68,70-72,75-84
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

4. ☒ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☒ the claims, Nos. 1-58, 61-68, 70-72, 75-84
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement:**

Novelty (N)	Claims	<u>12-13, 15-24,27, 31, 34,59,60,69,73,74</u>	YES
	Claims	<u>1-11,14 ,33</u>	NO
Inventive step (IS)	Claims	<u></u>	YES
	Claims	<u>1-24,27,31,33-34,59-60,69,73,74</u>	NO
Industrial applicability (IA)	Claims	<u>1-24,27,31,33-34,59-60,69,73,74</u>	YES
	Claims	<u></u>	NO

2. Citations and explanations (Rule 70.7)

The following documents(D) are considered to be relevant:

D1 : Bioorganic & Medicinal Chemistry Letters, 9(23), 3319-3324(1999);

D2: Journal of Natural Products, 64(7), 958-960(2001);

D3: Heterocycles, 29(2), 365-380(1989);

D6: EP-A1-0148660;

D7: CN-A-1358720;

Novelty (Art. 33(2) PCT)

D1 discloses Compound 20(Page 3320), D2 discloses Compound 25(Page 959, Table 2), D3 discloses Compounds 7-8, 10-13(Page 366 Table 1), the above compounds fall within the range of present claims 1-3, 5-6, 8, 10. The above compounds 7-8, 10-13 described in D3 falls within the range of present claims 4,7,9,11,14(The applicant's attention is drawn to the fact that sulfonic acid is a kind of organic acid containing one or more sulfonic groups, and CF_3SO_3^- is a kind of sulfonic radical). D1 discloses that compound 20 showed strong cytotoxic effects against KB and 1A9 cell lines(page 3323, paragraph 1 lines 6-7). That is to say, the subject-matter of claims 1-11, 14, 33 is respectively disclosed as a whole in D1~D3. Therefore claims 1-11, 14, 33 lacks novelty under Art. 33(2) PCT.

The subject-matter of claims 12-13, 15-24, 27, 31, 34, 59, 60, 69, 73, 74 is not disclosed in the available prior art , and is therefore novel.

Inventive step (Art. 33(3) PCT)

The subject-matter of claims 1-11, 14, 33 which lacks novelty is of course obvious to the person skilled in the art and therefore does not involve an inventive step under Art. 33(3)PCT.

D1 discloses that compound 20 showed strong cytotoxic effects against KB and 1A9 cell lines(page 3323, paragraph 1 lines 6-7), D7 discloses compounds of formula (I) for treatment of cancer(claims 1, 19, 20). The difference in terms of features between the novel

To be continued...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of Box No. V:

compounds of the present claims 1-19, 59-60, 69 and those of D1 and D7 lies in the substituents attached to the β -carboline. There is no evidence suggests that, compared with compounds of D1 or D7, compounds of the present claims has more potent anti-cancer activity or lowered toxicity. It is considered that the skilled man would have regarded the compounds of present claims 1-19, 59-60, 69 as obvious alternatives to the known compounds of D1 or D7. Consequently, it is considered that claims 1-19, 59-60, 69—as far as they are novel—do not involve an inventive step under Art. 33(3)PCT.

D1 discloses a process for preparation of compounds 12-14, including N-alkylation of compound 3 in THF-DMF in the present of 1.2 equiv. of NaH, 10 equiv. of CH_3I , $\text{C}_2\text{H}_5\text{I}$ or $\text{CH}_3(\text{CH}_2)_3\text{I}$ at room temperature over 3 hours (the last three lines of page 3319, page 3320 scheme 1). In light of D1, it is considered that the skilled man would have regarded the process of claim 20 as obvious. Therefore claim 20 does not involve an inventive step under Art. 33(3)PCT.

Likewise claims 22, 23, 27, 73, 74 do not involve an inventive step under Art.33(3)PCT.

D7 discloses a process for preparation of compounds of formula (I) (claim 18), In light of D7, it is considered that the skilled man would have regarded the processes of claim 21 and 24 as obvious. Therefore claim 21 and 24 do not involve an inventive step under Art. 33(3)PCT.

D6 discloses compound of formula(IV) (page3 and example 2). The difference in terms of features between the compounds(53a-55a) of present claim 31 and compound of formula(IV) of D6 lies in substituents attached to position 9 of the β -carboline. It is considered that the skilled man would have regarded the compounds of present claim 31 as obvious alternatives to the known compounds of D6. Consequently, it is considered that claims 31 does not involve an inventive step under Art. 33(3)PCT.

D1 discloses compound 20 and its strong cytotoxic effects against KB and 1A9 cell lines, D7 discloses compounds of formula (I) and their use for treatment of cancer. In light of D1 or D7, the novel subject matter of claim 33 and claim 34 is obvious to the person skilled in the art. Therefore claim 33 and 34 do not involve an inventive step under Art. 33(3)PCT.

Industrial applicability (Art. 33(4) PCT)

The compounds of claims 1-19, 31, 59-60, 69, the processes of claims 20-24, 27,73,74 and the uses of claims 33-34 can be used in the pharmaceutical industry (Art. 33(4) PCT).

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

It is noted that in present claims 1 no definition of the group X^- is given (Article 6 PCT; clarity). This report is completed for claim 1 wherein X^- is halogen, sulfonic group, sulfuric group, nitric group as defined in present description page 3.

R_7 and R_9 of the formula in description page 77 is not in consistent with R_4 and R_5 in table 34 (Article 6 PCT; clarity).

The formula in description page 77, 90, 94 substantively represents a cation, and there is no anion in the formula (Article 6 PCT; clarity).

The subject matter of claim 20 is a process for preparation of compounds of claim 1, but only part of compounds of claim 1 can be prepared with reactants described in claim 20, therefore the scope of claim 20 is unclear. Likewise, the scopes of claims 24, 27, 73, 74 are unclear (Article 6 PCT; clarity).

The subject matter of claim 23 is a process for preparation of compounds of claim 1, but only ethyl 9-substituted 1-methyl- β -carboline-3-carboxylate is prepared by step 5). That is to say on compounds of claim 1 that methyl is attached to position 1 of β -carboline can be prepared. Therefore, The scope of claim 23 is unclear (Article 6 PCT; clarity).

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

In claim 1 as originally filed, R_1 was defined as representing "... (second or tertiary) C_{1-6} -straight alkyl or second or tertiary branched alkyl... or 1-5 halo-substituted aralkyl...", and the corresponding passages of the description as originally filed defined the said group R_1 as representing "... C_{1-6} -primary, second or tertiary straight alkyl or second or tertiary branched alkyl... or 1-5 halo-, nitro-, or amino- aralkyl...". In current claim 1 there introduced definition of R_1 as representing "... straight or branched C_{1-6} -alkyl ... mono- or poly- substituted C_{6-10} -aralkyl...; wherein the substituents are defined as representing C_{1-4} -straight or branched alkyl, C_{1-4} -straight or branched alkoxy... hydroxy, carboxy".

In claim 1 and corresponding part of the description as originally filed, R_2 was defined as representing "... C_{1-6} -alkoxycarbonyl, aroxy carbonyl...". In current claim 1 there introduced definition of R_2 as representing "... straight or branched C_{1-6} -alkoxycarbonyl, C_{6-10} -aralkyloxycarbonyl, mono- or poly- substituted C_{6-10} -aralkyloxycarbonyl...; wherein the substituents are defined as above".

In claim 1 and corresponding part of the description as originally filed, R_3 was defined as representing "... C_{1-6} -alkoxy... aralkyloxy...". In current claim 1 there introduced definition of R_3 as representing "... straight or branched C_{1-6} -alkoxy, C_{6-10} -aralkyloxy".

In claim 1 and corresponding part of the description as originally filed, R_4 was defined as representing "... C_{1-6} -alkyl, C_{1-6} -hydroxyalkyl, C_{6-10} -aralkyl or 1-5 halo-substituted aralkyl...". In current claim 1 there introduced definition of R_4 as representing "... straight or branched C_{1-6} -alkyl, straight or branched C_{1-6} -hydroxyalkyl, mono- or poly- substituted C_{6-10} -aralkyl... wherein the substituents are defined as above".

In claim 1 as originally filed, R_5 was defined as representing "... C_{6-10} -aralkyl and 1-5 substituted aralkyl...", and the corresponding passages of the description as originally filed defined the said group R_5 as representing "... C_{6-10} -aralkyl and 1-5 substituted aralkyl, aryl-hydroxyl, aryl-carboxy, aryl-ester, aryl-amino, aryl-nitro...". In current claim 1 there introduced definition of R_5 as representing "... mono- or poly- substituted C_{6-10} -aralkyl; wherein the substituents are defined as above".

In the description as originally filed, X was defined as representing "halogen, sulfonic group, sulfuric group or nitric group". In current claim 1 there introduced definition of X as representing "pharmacologically acceptable organic or inorganic acid radicals; wherein the organic acids include Lewis acid".

In current claim 1 there introduced new definition of "Neither R_5 nor X exists".

" R_1 , R_2 , R_3 and R_4 are not all hydrogen" in claim 1 and corresponding part of the description as originally filed was changed in current claim 1 into " R_1 , R_2 , R_3 , R_4 , R_5 are not all hydrogen".

To be continued...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of Supplemental Box Sheet 2:

"R₁ is not methyl and R₃ is not methoxyl when R₂ and R₄ are hydrogen," in claim 1 and corresponding part of the description as originally filed was changed in current claim 1 into "R₁ is not methyl and R₃ is not methoxyl when R₂, R₄ and R₅ are hydrogen".

"R₂, R₃ and R₄ are not all hydrogen when R₁ is methyl" in claim 1 and corresponding part of the description as originally filed was changed in current claim 1 into "R₂, R₃, R₄ and R₅ are not all hydrogen when R₁ is methyl".

"R₄ is not methyl, ethyl or butyl when R₁ is methyl, R₂ is hydrogen and R₃ is methoxyl" in claim 1 and corresponding part of the description as originally filed was changed in current claim 1 into "R₄ is not methyl, ethyl or butyl when R₁ is methyl, R₂ and R₅ are hydrogen, and R₃ is methoxyl".

"R₂ is not methoxylcarbonyl and R₄ is not methyl when R₁ and R₃ are methyl" was deleted in current claim 1.

All of the above amendments go beyond the disclosure of the international application as originally filed.

Claims 2-42 which refer to claim 1 include part of above subject matter content that goes beyond the disclosure of the international application as originally filed.

Furthermore, the definition of the following groups in current claims goes beyond the disclosure of the international application as originally filed,

Definition of R₁ as representing C₁₋₆-straight or branched alkyl; C₆₋₁₀-aryl-C₀₋₆-straight or branched alkyl; mono- or poly-substituted C₆₋₁₀-aryl-C₀₋₆-straight or branched alkyl; C₁₋₄-straight or branched alkyl; C₆₋₁₀-aryl-C₀₋₄-straight or branched alkyl; mono- or poly-substituted C₆₋₁₀-aryl-C₀₋₄-straight or branched alkyl; phenyl-C₀₋₄-straight or branched alkyl; mono- or poly-substituted phenyl-C₀₋₄-straight or branched alkyl; phenyl; mono- or poly-substituted phenyl; phenyl-C₀₋₂-alkyl; or mono- or poly-substituted phenyl-C₀₋₂-alkyl;

Definition of R₂ as representing C₁₋₆-straight or branched alkoxy carbonyl; C₆₋₁₀-aryl-C₁₋₆-straight or branched alkoxy carbonyl; mono- or poly-substituted C₆₋₁₀-aryl-C₁₋₆-straight or branched alkoxy carbonyl; C₁₋₄-straight or branched alkoxy carbonyl; phenyl-C₁₋₄-alkoxy carbonyl; mono- or poly-substituted phenyl-C₁₋₄-alkoxy carbonyl; neither R₅ nor X exists when R₂ is metallic carboxylates; alkali metallic carboxylates, wherein alkali metal is lithium, sodium, potassium, rubidium, cesium; sodium carboxylate or potassium carboxylate; C₆₋₁₀-aryl-C₁₋₄-straight or branched alkoxy carbonyl; mono- or poly-substituted C₆₋₁₀-aryl-C₁₋₄-straight or branched alkoxy carbonyl; alkali metallic carboxylates; COOM, wherein M is metal, sodium, potassium;

Definition of R₃ as representing C₁₋₆-straight or branched alkoxy; C₆₋₁₀-aryl-C₁₋₆-straight or branched alkoxy; C₁₋₄-straight or branched alkoxy; C₁₋₂-alkoxy;

To be continued...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of Supplemental Box Sheet 3:

Definition of R_4 as representing C_{1-6} -straight or branched alkyl; hydroxyl- C_{1-6} -straight or branched alkyl; C_{6-10} -aryl- C_{1-6} -straight or branched alkyl; mono- or poly-substituted C_{6-10} -aryl- C_{1-6} -straight or branched alkyl; C_{1-4} -straight or branched alkyl; hydroxyl- C_{1-4} -straight or branched alkyl; C_{6-10} -aryl- C_{1-4} -straight or branched alkyl; mono- or poly-substituted C_{6-10} -aryl- C_{1-4} -straight or branched alkyl; phenyl- C_{1-4} -straight or branched alkyl; mono- or poly-substituted phenyl- (C_{1-4}) -straight or branched alkyl; phenyl- C_{1-2} -alkyl; or mono- or poly-substituted phenyl- C_{1-2} -alkyl;

Definition of R_5 as representing C_{6-10} -aryl- C_{1-6} -straight or branched alkyl; mono- or poly-substituted C_{6-10} -aryl- C_{1-6} -straight or branched alkyl; straight or branched C_{1-4} -alkyl; C_{6-10} -aryl- C_{1-4} -straight or branched alkyl; mono- or poly-substituted C_{6-10} -aryl- C_{1-4} -straight or branched alkyl; C_{2-3} -straight or branched alkyl; phenyl- C_{1-4} -straight or branched alkyl; mono- or poly-substituted phenyl- C_{1-4} -straight or branched alkyl; phenyl- C_{1-2} -alkyl; mono- or poly-substituted phenyl- C_{1-2} -alkyl; mono- or poly-halo-benzyl; C_{3-4} -straight or branched alkyl; straight or branched butyl; R_5 does not exist;

Definition of X as representing phosphoric radical; chlorine; or does not exist.

The above definition which goes beyond the disclosure of the international application as originally filed also make current claims 2-5, 9-12, 15, 17-19, 21-24, 29-34, 37-40, 43-58 unacceptable.

"Pharmacologically acceptable salts" in current claim 61, "wherein the Pharmacologically acceptable salt is hydrochloride" in current claim 63, "carboxylates are metallic carboxylates" in current claim 64, "the metal is alkali metal" in current claim 65, "alkali metal is sodium or potassium" in current claim 66, "alkali metal is sodium" in current claim 67, "alkali metal is potassium" in current claim 68 all goes beyond the disclosure of the international application as originally filed.

Claim 70 refers to claim 1, therefore the scope of definition of substituents at position 9 of β -carboline goes beyond the disclosure of the international application as originally filed.

Claims 71 and 72 refer to claim 1, therefore the definition of R , R_1 , R_3 , R_4 , R_5 , X in claims 71 and 72 and the definition of M in claim 71 go beyond the disclosure of the international application as originally filed.

The step 2), step 5), step 6) and step 7) introduced into claim 71 and step 6) into claim 72 go beyond the disclosure of the international application as originally filed.

The reaction condition introduced into step 1) and step 3) of claim 71 and reaction condition introduced into step 5 and 6 in claim 72 go beyond the disclosure of the international application as originally filed.

To be continued.....

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of Supplemental Box Sheet 4:

Definition of R₉ as representing mono-substituted benzyl or mono-substituted phenylpropyl in claim 75 go beyond the disclosure of the international application as originally filed.

The introduction of subject matter content of claim 76 goes beyond the disclosure of the international application as originally filed.

The introduction of "tumor of alimentary tract", "oral cancer", "oesophagus cancer" "intestinal cancer" into claim 78, "prostatic cancer" into claim 80, "oophoroma" into 82 go beyond the disclosure of the international application as originally filed.

Directly or indirectly referring to claims 1-69 makes claims 76-84 unacceptable.

Therefore, the subject matter content of current claims 1-58, 61-68, 70-72, 75-84 goes beyond the disclosure of the international application as originally filed(Art.34(2)(b)PCT). This report is established as if the above amendments had not been made. This report is based on claims 1-24, 27, 31, 33-34 as originally filed; claims 59-60, 69, 73-74 received by this Authority on 29. Dec. 2004.